

clearly inadequate for the purposes at hand. Rather fine categorisation is used for husband's occupation, but analysis of the data does not indicate that this is a significant predictor. The stratification for age, on the other hand, is far too coarse. Variations of cancer incidence within 10-year age ranges are large compared with the variations attributed to the husband's smoking. Even relatively small differences in the age distribution of the three populations could thus produce the reported apparent effect. The use of husbands' rather than wives' ages for stratification compounds the problem.

The measure of risk is also inappropriate for a study of such extended duration. The number of person years at risk rather than the number of subjects should be used as the exposure variable, since many subjects would have died of other causes during the study. The appropriate procedure for analysing data of this type is given in Mantel's original paper.¹

Finally, it is clear from the original paper that Dr Hirayama analysed several causes of death, but reported statistics only for lung cancer. The procedure of reporting only the most significant result from a choice of several possible dependent measures a posteriori is a common error which naturally leads to inflated estimates of significance. Only an appropriate multivariate test can properly estimate statistical significance in this situation.

The analysis reported must thus be regarded as inconclusive unless more refined analyses are able to confirm the results. We endorse the author's suggestion that further study based on larger samples is needed, but we emphasise that such studies can be useful only if the relevant biomedical data are recorded and analysed in sufficient detail to isolate the hypothesised effect from confounding factors.

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¹ Mantel N, Haipertin M. *Journal of the American Statistical Association* 1963;58:611-27.

SIR.—Most of the questions raised in my letter (3 October, p 917) were not addressed in the response of Dr Hirayama that followed. The first readings of his original paper troubled me in view of his recognised work, so that before I commented I reviewed every Hirayama paper in the literature on this study population to see if the collective information might answer the questions. A map of Japan was constructed by prefectures and minor population subdivisions and the areas of the study were marked as nearly as they could be ascertained. Review of the reports on the epidemiology and clinical aspects of lung cancer of other Japanese scientists and finally a serious study of Japanese demography, industry, disease trends, and all pertinent data were made; so the questions asked were serious and responsible.

Dr Hirayama did not answer the question about how or why the specific health stations surveyed were selected, or how the few prefectures of the total in Japan from which the health stations were chosen were selected. He admitted that the selection was not random and stated, "The satisfactory representativeness of the sample was confirmed after the survey."

He does not say by what criteria this was confirmed.

Mapping of the areas selected for study and of the industrial concentrations shows them to be related in nearly every instance. Dr Hirayama states, "Asbestos exposure is quite unlikely to have influenced our result since the proportion of industrial areas are surely not in excess in our sample." Asbestos and other industrial exposures would have to be considered according to the locations of the study areas and of the industrial complexes as revealed on the map of Japan. The areas were nearly all in the areas with high standardised mortality ratios in the excellent and fully documented countrywide epidemiological lung cancer mortality study of Minowa *et al.*¹ The tabulation on the basis of the husbands' ages is not explained. According to the median age at time of marriage in Japan, there is a difference between husbands' and wives' ages, the wives being generally younger. Dr Hirayama states, "We have tables by wives' ages separately." They were not found in the literature search on these data.

No response at all was made to the following questions: (1) Were the families whose medical care was covered by industry omitted from the study? (2) To what population is Hirayama referring? (3) Why were 31% of the women surveyed (and 40% of the women smokers) listed as unknown or not specified as to occupation? For a person to person survey, this suggests methodological problems. (4) Why were references to current Japanese studies by reputable men, Minowa *et al.*¹ and Aoki,² whose findings did "not seem to explain the prefectural differences of lung cancer mortality" not mentioned? (5) The report by Ishikawa³ on the preponderance of adenocarcinoma in Japan, in a footnote of which he acknowledges the assistance of Dr Hirayama, his colleague as a reviewer, is not referred to in the answer, although this is very important to this discussion.

Two new issues were introduced by Dr Hirayama in his response, one on the quantity of sidestream smoke inhaled by the wives, without any discussion of the quantity smoked in houses or in the presence of the wives. All the sidestream smoke of husbands' cigarettes would not be inhaled. A remarkably careful study on this subject was reported in 1978 by a French group that helps to explain the differences reported by different techniques of measurement. They improved and explained each innovation they used to overcome logistical problems noted in previous studies. They concluded, with valid proof, that on the strictly toxicological level there is no hazard for non-smokers. The report does not neglect to remark on the problems that are presented to a very important fraction of the population, however. The second issue introduced in the reply was that inhalation through the nose is different from the smoker's direct inhalation. This did not consider the superb filtering system, which would conceivably reduce the amount of ambient smoke inhaled by the wives.⁴

Finally, the far-reaching implications of this

unproved passive smoking effect are already in evidence in the literature.

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¹ Minowa M, Shigematsu I, Nagai M, Fukutomi K. *Soc Sci Med* 1981;15D(1):225-31.
² Aoki K, Ohno Y. *Nippon Rinsho* 1980;38:2541-50.
³ Ishikawa S. *Jpn J Clin Oncol* 1973;3:19-30.
⁴ Badre R, Guillemet R, Abran N, Bourdin M, Dumas C. *Annales Pharmaceutiques Françaises* 1978;36:443-52.

SIR.—Dr T Hirayama (17 January, p 183) reports a greater risk of lung cancer in non-smoking women when their husbands smoke than when they do not. Assessing the statistical significance of this association by a χ^2 trend statistic on one degree of freedom, Dr N Mantel (3 October, p 914) showed that a non-significant value of 3.31 is obtained if age and occupation are ignored. However, if these factors are taken into account, on the basis of data given in table I of Dr Hirayama's recent letter (3 October, p 916), a higher χ^2 value of 8.70 is obtained, which is statistically significant ($p < 0.01$), and similar to, though not identical with, the value of 10.88 given in his original paper. While this slight discrepancy might have been due, perhaps, to the use of narrower age bands in Dr Hirayama's original calculations, it is clear that the much more significant differences claimed in tables II and III of his letter are due to a statistical error.

Table II, which gives a very much higher χ^2 value of 36.81 for a similar comparison, is based on the false assumption that the lung cancer rate of non-smoking women with husbands who did not smoke is known precisely. The correct calculation, given in my table, gives a much lower level of significance for the Japanese data, and his calculations for the American¹ and Greek² data are similarly in error. Consideration only of women with smoking husbands has also led Dr Hirayama to conclude incorrectly that the American study was materially less powerful than the Japanese study because of sample size. In fact, the studies were of very similar power, a slightly smaller total number of deaths in the American study (153 compared with 174) being balanced by the greater stability of the denominator in the relative risk calculations, due to the greater number of deaths in women whose husbands did not smoke (65 compared with 32).

The source of the error in his table III is not clear, but the remarkably narrow 95% confidence bands for relative risk given in the table below the figure cannot be even approximately correct. How, for example, can the ratio of 2.94 given for the comparison of lung cancer rates between non-smoking men whose wives smoke (seven deaths out of 1010) and non-smoking men whose wives do not smoke (50 deaths out of 19 279) possibly have 95% limits as close together as 2.65 and 3.26—that is, $\pm 10\%$ —when the 95% limits for the seven observed deaths are approximately 2 and 12—that is, $\pm 70\%$ —and the variability of the relative risk must be greater than this?

Hugod, *et al.*³ have shown that under quite extreme passive smoke conditions, sufficient to produce a carbon monoxide air concentration of 20 parts per million, a non-smoker would take 11

Observed and expected deaths from lung cancer in non-smoking women in the Japanese study according to the smoking habit of their husbands

	Husbands do not smoke		Husbands smoke		χ^2	P
	Observed	Expected	Observed	Expected		
As given by Hirayama	32	(32.0)	142	85.8	36.81	<0.0001
Correct calculation	32	45.8*	142	128.2*	5.78	<0.05

* Standardised for age and occupation on the basis of data in table I of Dr Hirayama's letter (3 October, p 916).

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